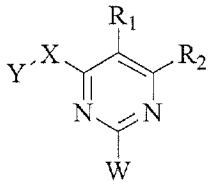
AMENDMENTS TO THE CLAIMS

1. (Currently amended) A compound having the formula I:



(I)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt~~, ester, or prodrug~~ thereof, wherein

Y is selected from the group consisting of

(1) substituted or unsubstituted aryl,

(2) substituted or unsubstituted heterocyclyl, and

(3) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

(1) a direct link,

(2) $-N(R^{1x})-$,

(3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$,

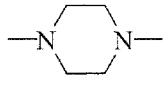
(4) -O-,

(5) -S-,

(6) -SO-,

(7) $-SO_2-$,

(8) $-C(R^{2x}, R^{3x})-$, and

(9)  ,

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

(a) H,

(b) substituted or unsubstituted C_1-C_6-alkyl,

(c) substituted or unsubstituted C_2-C_6-alkenyl,

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(d) substituted or unsubstituted C_2-C_6-alkynyl,

(e) substituted or unsubstituted aryl,

(f) substituted or unsubstituted heterocyclyl,

(g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R_1 is selected from the group consisting of

(1) H,

(2) substituted or unsubstituted C_1-C_6-alkyl,

(3) -COOH,

(4) halo,

(5) $-OR^{1t}$, and

(6) $-NHR^{1t}$,

wherein R^{1t} is H or C_1-C_6-alkyl;

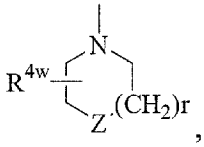
R_2 is selected from the group consisting of

(1) substituted or unsubstituted aryl,

(2) substituted or unsubstituted heteroaryl, and

W is selected from the group consisting of

(1) $-N(R^{1w}, R^{2w})$, and

(2) 

,

wherein R^{1w} and R^{2w} are selected from the group consisting of

(a) substituted or unsubstituted aryl,

(b) substituted or unsubstituted heterocyclyl, and

(c) substituted or unsubstituted heteroaryl,

Z is selected from the group consisting of

(a) -O-,

(b) $-NR^z-$,

(c) -S-,

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(d) -SO-,

(e) $-SO_2-$, and

(f) $-CH_2-$,

wherein R^z is H or substituted or unsubstituted alkyl group; and

R^{4w} is selected from the group consisting of

(a) H,

(b) substituted or unsubstituted C_1-C_6-alkyl,

(c) $-COOR^{5w}$,

(d) $-CONH_2$,

(e) $-OR^{5w}$, and

(f) $-NHR^{5w}$,

wherein R^{5w} is H or C_1-C_6-alkyl; and r is 0, 1, or 2;

with the proviso that when R_2 is phenyl independently substituted with one to five substituents selected from hydrogen, cycloalkyl, heterocycloalkyl, halo, nitro, amino, sulphonamido, or alkylsulphonylamino, R_1 is hydrogen, haloalkyl, alkyl, or halo, and X is NR^{1x}, then Y is substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocyclyl.

2. (Previously presented) The compound of claim 1, wherein

Y is selected from the group consisting of

(1) substituted or unsubstituted aryl,

(2) substituted or unsubstituted heterocyclyl, and

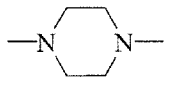
(3) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

(1) a direct link,

(2) $-N(R^{1x})-$,

(3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and

(4)  ,

wherein R^{1x}, R^{2x}, R^{3x} are independently H or substituted or unsubstituted C_1-C_6-alkyl; and

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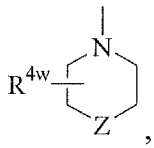
W is selected from the group consisting of



wherein Z is -O- or -NR^z-, wherein R^{4w} is H or substituted or unsubstituted C_1-C_6-alkyl.

3. (Original) The compound of claim 1, wherein

Y is selected from the group consisting of

(1) substituted or unsubstituted heterocyclyl,

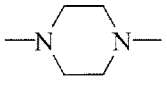
(2) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

(1) a direct link,

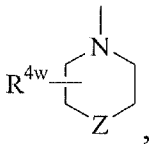
(2) -$N(R^{1x})$-,

(3) -$(CH_2)_m$-$C(R^{2x}, R^{3x})$-$N(R^{1x})$-, and

(4)  ,

wherein R^{1x}, R^{2x}, R^{3x} are independently H or substituted or unsubstituted C_1-C_6-alkyl; and

W is selected from the group consisting of



wherein Z is -O- or -NR^z-, wherein R^{4w} is H or substituted or unsubstituted C_1-C_6-alkyl.

4. (Original) The compound of claim 1, wherein

Y is substituted or unsubstituted aryl;

X is selected from the group consisting of

(1) a direct link,

(2) -$N(R^{1x})$-,

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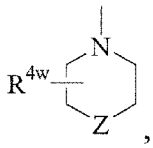
(3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and

(4)  ,

wherein R^{1x}, R^{2x}, R^{3x} are independently H or substituted or unsubstituted C_1-C_6-alkyl; and

W is selected from the group consisting of

 ,

wherein Z is -O- or $-NR^z-$, wherein R^{4w} is H or substituted or unsubstituted C_1-C_6-alkyl.

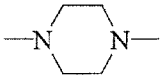
5. (Previously presented) The compound of claim 1, wherein

X is selected from the group consisting of

(1) a direct link,

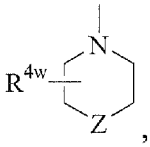
(2) $-N(R^{1x})-$,

(3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and

(4)  ,

wherein R^{1x}, R^{2x}, R^{3x} are independently H or substituted or unsubstituted C_1-C_6-alkyl; and

W is selected from the group consisting of

 ,

wherein Z is -O- or $-NR^z-$, wherein R^{4w} is H or substituted or unsubstituted C_1-C_6-alkyl.

6. (Original) The compound of claim 1, wherein

Y is selected from the group consisting of

(1) substituted or unsubstituted heterocyclyl,

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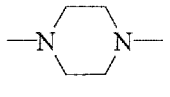
(2) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

(1) a direct link,

(2) $-N(R^{1x})-$,

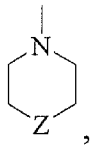
(3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and

(4)  ,

wherein R^{1x}, R^{2x}, R^{3x} are independently H or substituted or unsubstituted C_1-C_6-alkyl;

R_2 is substituted or unsubstituted aryl; and

W is

 ,

wherein Z is -O- or -NH-.

7. (Original) The compound of claim 1, wherein

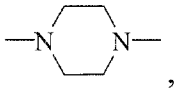
Y is substituted or unsubstituted aryl;

X is selected from the group consisting of

(1) a direct link,

(2) $-N(R^{1x})-$,

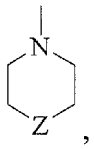
(3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and

(4)  ,

wherein R^{1x}, R^{2x}, R^{3x} are independently H or substituted or unsubstituted C_1-C_6-alkyl;

R_2 is substituted or unsubstituted aryl; and

W is

 ,

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wherein Z is -O- or -NH-.

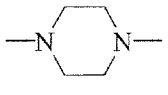
8. (Previously presented) The compound of claim 1, wherein

X is selected from the group consisting of

(1) a direct link,

(2) $-N(R^{1x})-$,

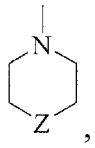
(3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and

(4)  ,

wherein R^{1x}, R^{2x}, R^{3x} are independently H or substituted or unsubstituted C_1-C_6-alkyl;

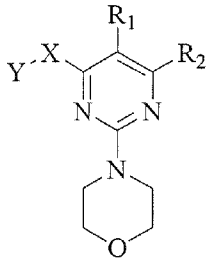
R_2 is substituted or unsubstituted aryl; and

W is

 ,

wherein Z is -O- or -NH-.

9. (Previously presented) The compound of claim 1, having the formula II:



(II)

wherein Y is selected from the group consisting of

(1) substituted or unsubstituted aryl,

(2) substituted or unsubstituted heterocyclyl, and

(3) substituted or unsubstituted heteroaryl; and

X is selected from the group consisting of

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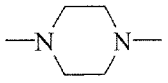
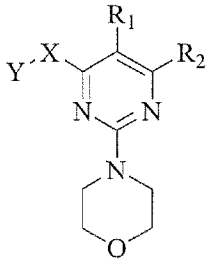
(1) a direct link,

(2) $-N(R^{1x})-$,

(3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and

(4)  .

10. (Original) The compound of claim 1, having the formula II:



(II)

wherein Y and X, taken together, are selected from the group consisting of

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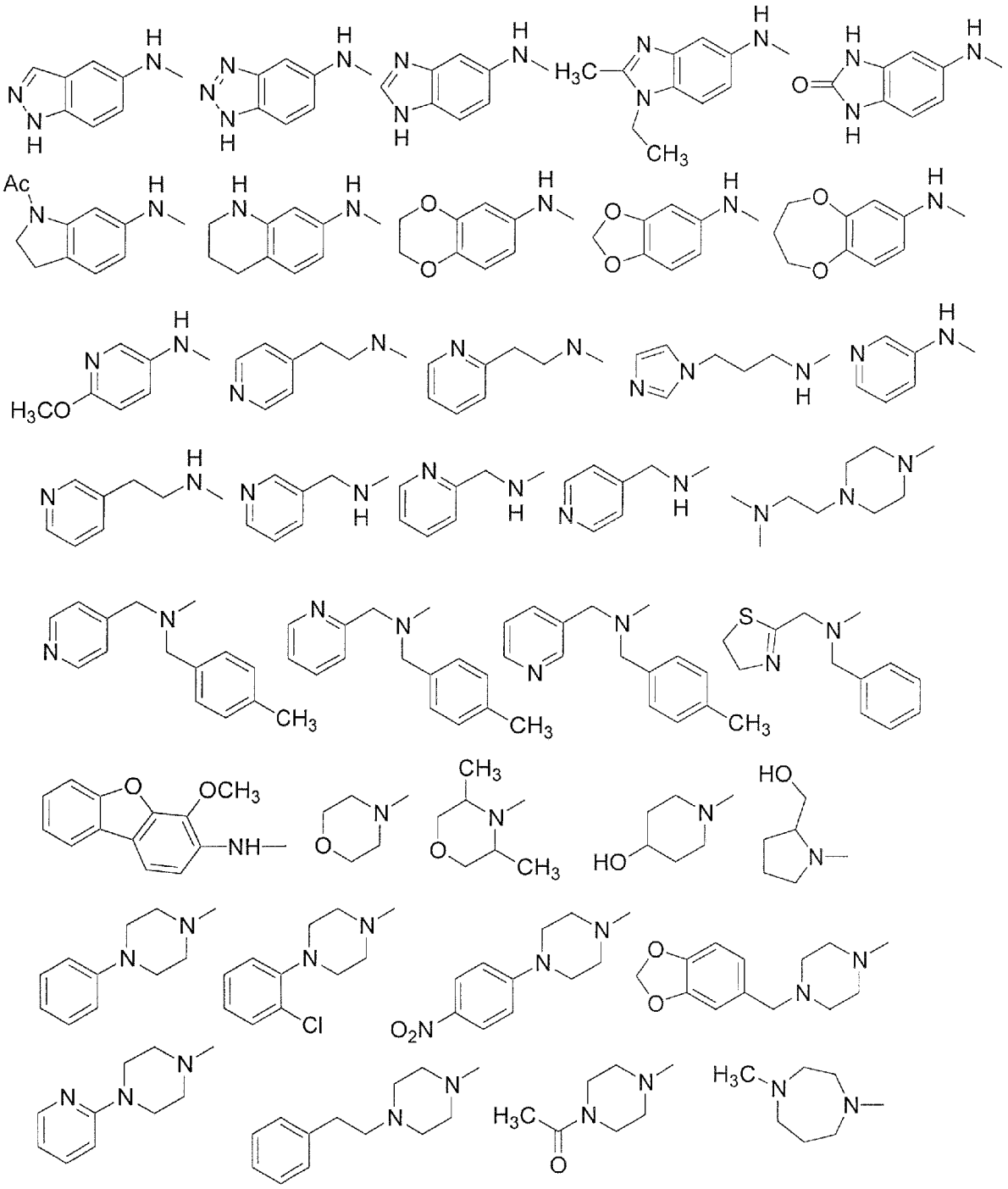

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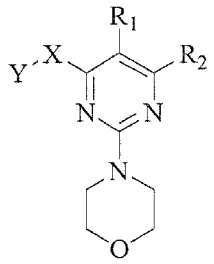
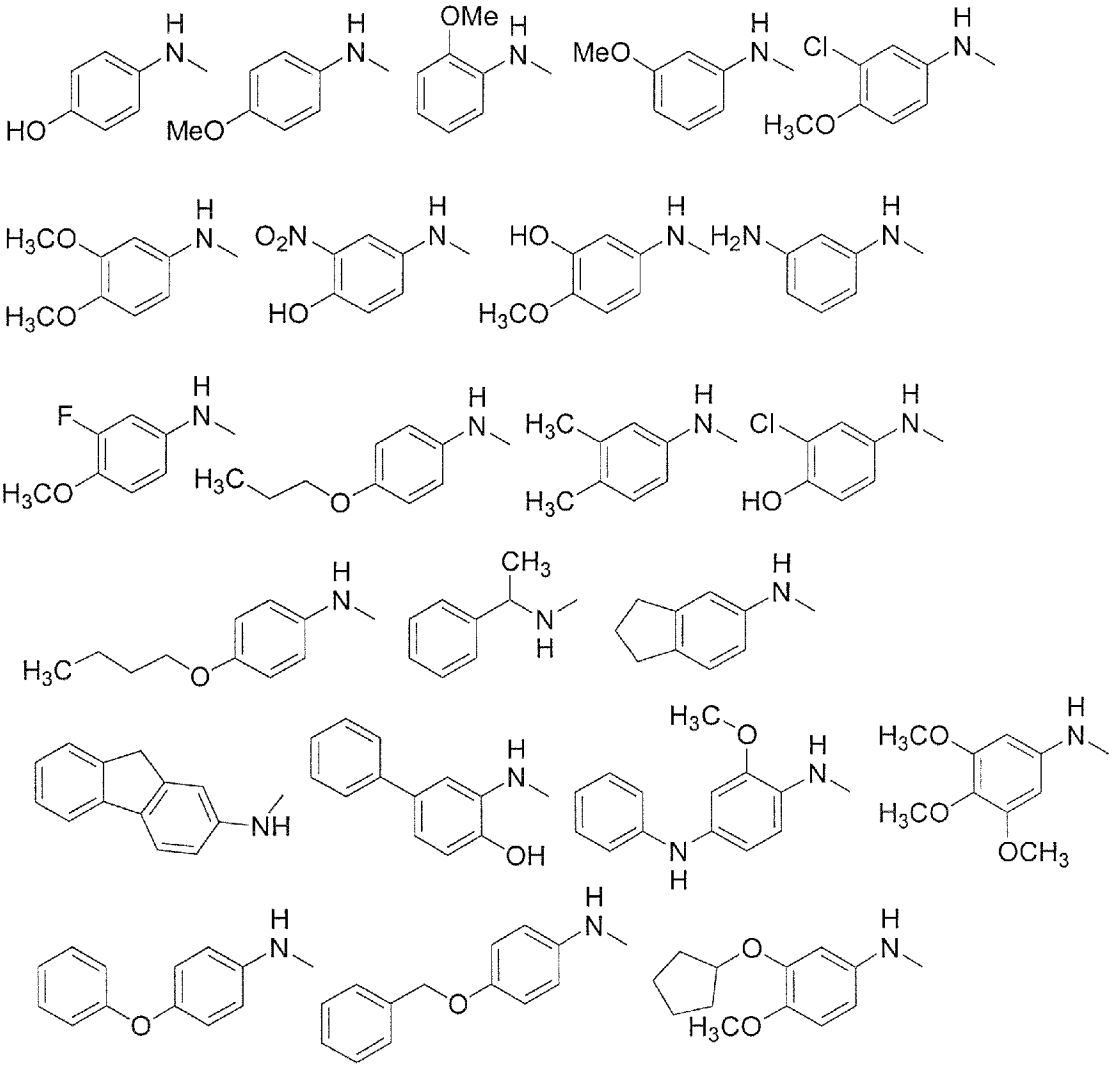
11. (Original) The compound of claim 1, having the formula II:



(II)

wherein Y and X, taken together, are selected from the group consisting of



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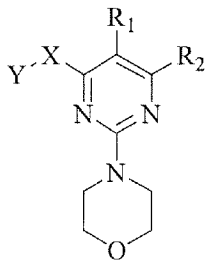
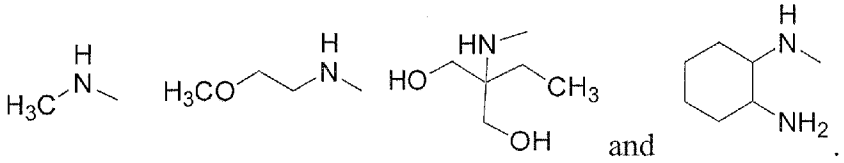
12. (Original) The compound of claim 1, having the formula II:



(II)

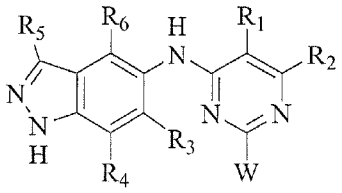
wherein, Y and X, taken together, are selected from the group consisting of



and

.

13. (Previously presented) The compound of claim 1, having the formula III:



(III)

wherein R_3, R_4, R_5, R_6 are selected from the group consisting of

(1) H,

(2) substituted or unsubstituted C_1-C_6-alkyl,

(3) -COORt[1],

(4) -$CONH_2$,

(5) -OR^{1t}, and

(6) -NHR^{1t}.

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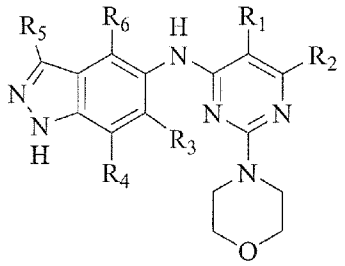
14. (Previously presented) The compound of claim 1, having the formula IV:



(IV)

wherein R_3, R_4, R_5, R_6 are selected from the group consisting of

(1) H,

(2) substituted or unsubstituted C_1-C_6-alkyl,

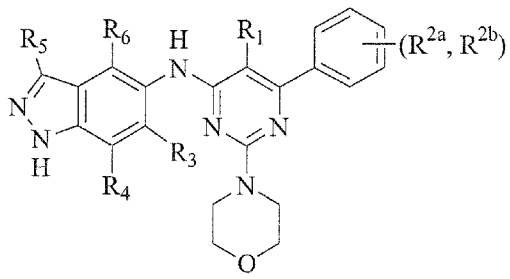
(3) -$COOR^{1t}$,

(4) -$CONH_2$

(5) -OR^{1t}, and

(6) -NHR^{1t}.

15. (Previously presented) The compound of claim 1, having the formula V:



(V)

wherein R_3, R_4, R_5, R_6 are selected from the group consisting of

(1) H,

(2) substituted or unsubstituted C_1-C_6-alkyl,

(3) -$COOR^{1t}$,

(4) -$CONH_2$

(5) -OR^{1t}, and

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(6) -NHR^{1t}; and

R^{2a} and R^{2b} are selected from the group consisting of

(1) H,

(2) substituted or unsubstituted alkyl,

(3) halo,

(4) $-(CH_2)_q-N(R^{2c}, R^{2d})$,

(5) $-(CH_2)_q-N(R^{2c}, R^{2d})COR^{2e}$,

(6) $-(CH_2)_q-OR^{2e}$,

(7) $-(CH_2)_q-OCOR^{2e}$,

(8) $-(CH_2)_q-OCOOR^{2e}$,

(9) $-(CH_2)_q-COOR^{2e}$,

(10) $-(CH_2)_q-CONR^{2c}$,

(11) -CN,

(12) $-NO_2$,

(13) $-SO_2NH_2$,

(14) $-NHSO_2CH_3$, and

(15) $-SO_2R^{2f}$,

wherein R^{2c}, R^{2d}, R^{2e}, and R^{2f} are selected from the group consisting of

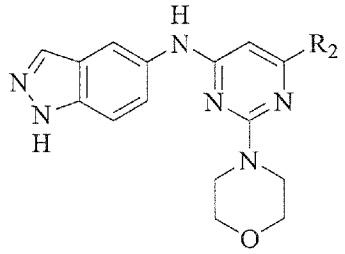
(a) H,

(b) substituted or unsubstituted alkyl, and

(c) substituted or unsubstituted phenyl; and

q is 0, 1, 2, 3, or 4.

16. (Original) The compound of claim 1, having the formula VI:



(VI)

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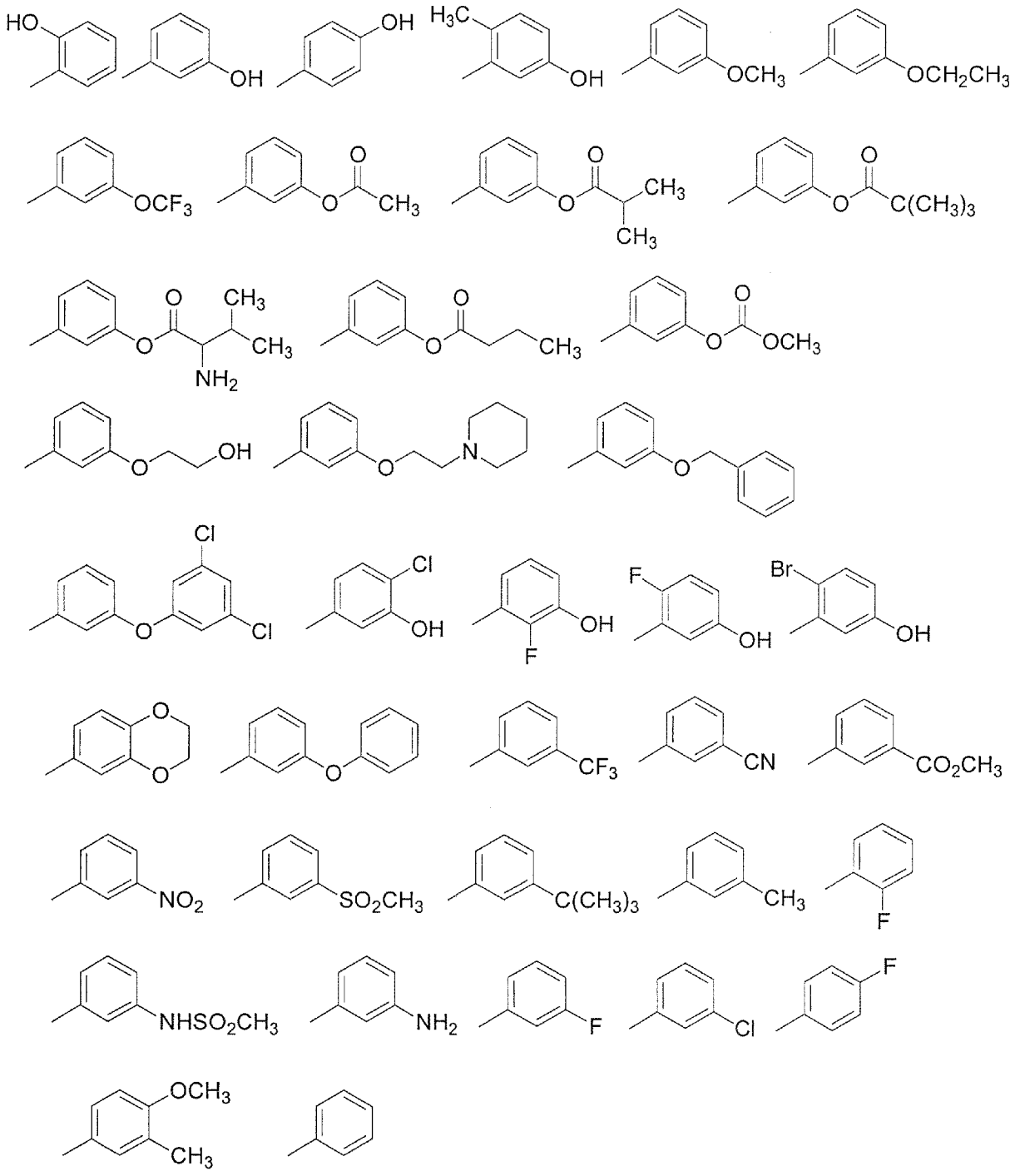
wherein R_2 is selected from the group consisting of



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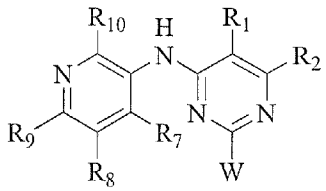
17. (Previously presented) The compound of claim 1, having the formula VII:



(VII)

wherein R_7, R_8, R_9, and R_{10} are selected from the group consisting of

(1) H,

(2) substituted or unsubstituted C_1-C_6-alkyl,

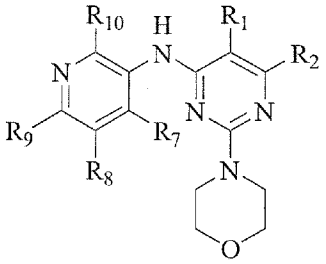
(3) $-COOR^{1t}$,

(4) $-CONH_2$

(5) $-OR^{1t}$, and

(6) $-NHR^{1t}$.

18. (Original) The compound of claim 1, having the formula VIII:



(VIII)

wherein R_7, R_8, R_9, R_{10} are selected from the group consisting of

(1) H,

(2) substituted or unsubstituted C_1-C_6-alkyl,

(3) $-COOR^{1t}$,

(4) $-CONH_2$,

(5) $-OR^{1t}$, and

(6) $-NHR^{1t}$.

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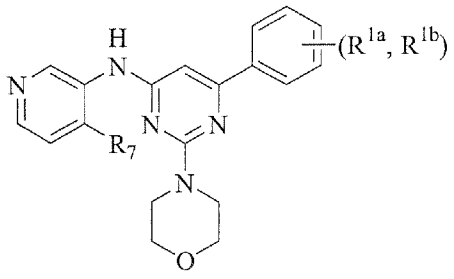
19. (Original) The compound of claim 1, having the formula IX:



(IX)

wherein R^{1a} and R^{1b} are selected from the group consisting of

(1) H,

(2) substituted or unsubstituted alkyl,

(3) halo,

(4) $-(CH_2)_q-N(R^{2c}, R^{2d})$,

(5) $-(CH_2)_q-N(R^{2c}, R^{2d})COR^{2e}$,

(6) $-(CH_2)_q-OR^{2e}$,

(7) $-(CH_2)_q-OCOR^{2e}$,

(8) $-(CH_2)_q-OCOOR^{2e}$,

(9) $-(CH_2)_q-COOR^{2e}$,

(10) $-(CH_2)_q-CONR^{2c}$,

(11) -CN,

(12) $-NO_2$,

(13) $-SO_2NH_2$,

(14) $-NHSO_2CH_3$, and

(15) $-SO_2R^{2f}$,

wherein R^{2c}, R^{2d}, R^{2e}, and R^{2f} are selected from the group consisting of

(a) H,

(b) substituted or unsubstituted alkyl, and

(c) substituted or unsubstituted phenyl; and

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wherein R_7 is selected from the group consisting of

(1) H,

(2) substituted or unsubstituted C_1-C_6-alkyl,

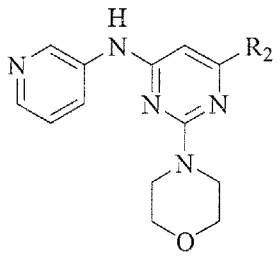
(3) $-COOR^{1t}$,

(4) $-CONH_2$,

(5) $-OR^{1t}$, and

(6) $-NHR^{1t}$.

20. (Original) The compound of claim 1, having the formula X:



(X)

wherein R_2 is selected from the group consisting of

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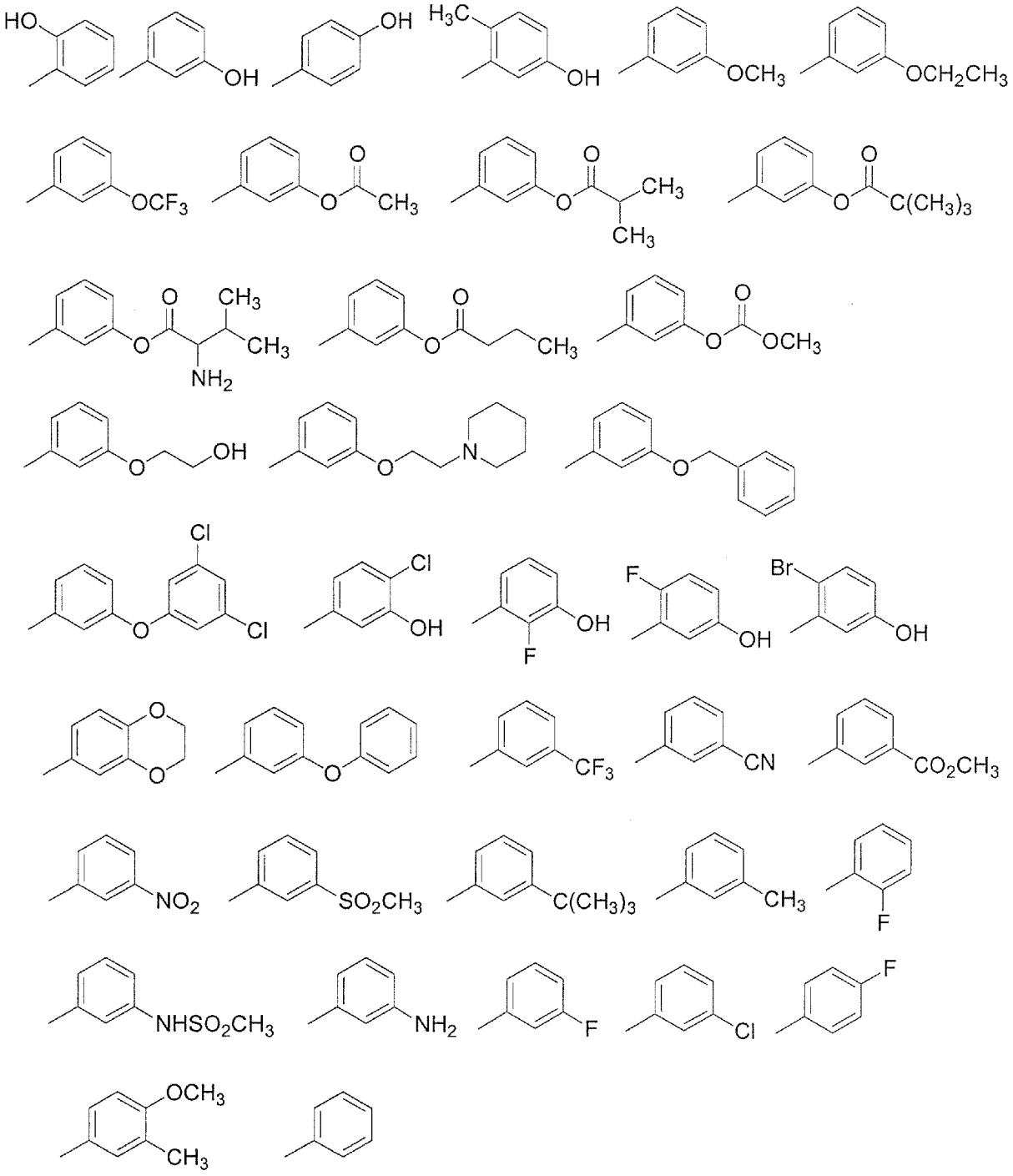

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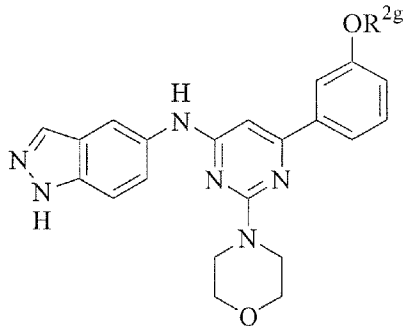
21. (Original) The compound of claim 1, having the formula XI:



(XI)

wherein R^{2g} is selected from the group consisting of

(1) H,

(2) substituted or unsubstituted alkyl,

(3) $-CONHR^{2h}$,

(4) $-CON(R^{2h})-(CH_2)_{2-3}-N(R^{2h}, R^{2i})$,

(5) $-COR^{2j}$,

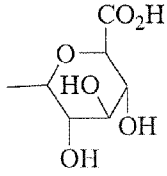
(6) $-CO_2R^{2j}$,

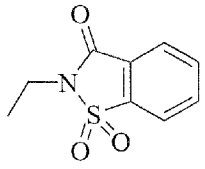
(7) $-COC_1-C_6$-alkyl-CO_2H,

(8) $-CH_2-OC(=O)R^{2i}$,

(9) $-CH_2-OC(=O)NHCHR^{2i}CO_2R^{2j}$,

(10) $-P(=O)(OR^{2k}, OR^{2p})$,

(11)  , and

(12)  ,

wherein R^{2h}, R^{2i}, R^{2j}, R^{2k}, and R^{2p} are selected from the group consisting of

(a) H,

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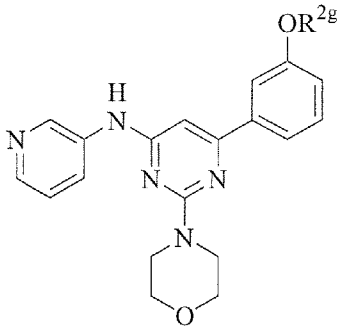
(b) substituted or unsubstituted alkyl, and

(c) substituted or unsubstituted aryl.

22. (Original) The compound of claim 1, having the formula XII:



(XII)

wherein R^{2g} is selected from the group consisting of

(1) H,

(2) substituted or unsubstituted alkyl,

(3) $-CONHR^{2h}$,

(4) $-CON(R^{2h})-(CH_2)_{2-3}-N(R^{2h}, R^{2i})$,

(5) $-COR^{2j}$,

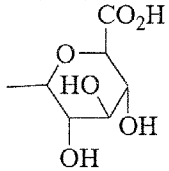
(6) $-CO_2R^{2j}$,

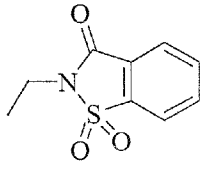
(7) $-COC_1-C_6$-alkyl-CO_2H,

(8) $-CH_2-OC(=O)R^{2i}$,

(9) $-CH_2-OC(=O)NHCHR^{2i}CO_2R^{2j}$,

(10) $-P(=O)(OR^{2k}, OR^{2p})$,

(11)  , and

(12)  ,

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wherein R^{2h}, R^{2i}, R^{2j}, R^{2k}, and R^{2p} are selected from the group consisting of

(a) H,

(b) substituted or unsubstituted alkyl, and

(c) substituted or unsubstituted aryl.

23. (Currently amended) A composition, comprising a compound of Claim 1 and a pharmaceutically acceptable carrier ~~and an amount of a compound of Claim 1 effective to inhibit phosphotidylinositol (PI) 3-kinase activity in a human or animal subject when administered thereto~~.

24. (Currently amended) The composition of Claim 23 further comprising at least one additional agent for the treatment of breast cancer.

25. (Currently amended) The composition of Claim 24, wherein the at least one additional agent for the treatment of breast cancer is selected from irinotecan, topotecan, gemcitabine, gleevec, herceptin, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab, tamoxifen, CPT 11, and trastuzumab.

26. (Currently amended) A method for treating ~~a condition by modulation of phosphotidylinositol (PI) 3-kinase activity~~ breast cancer comprising administering to a ~~human or animal~~ subject in need of such treatment an effective amount of a compound of Claim 1.

27. (Original) The method of Claim 26, wherein the compound has an IC_{50} value of less than about 20 μM in a cell proliferation assay.

28-30. (Canceled)

31. (Currently amended) The method of Claim [[30]] 26 further comprising administering to the human or animal subject at least one additional agent for the treatment of breast cancer.

32. (Currently amended) The method of Claim 31, wherein the at least one additional agent for the treatment of breast cancer is selected from irinotecan, topotecan, gemcitabine, gleevec, herceptin, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine,

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cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab, tamoxifen, CPT 11, and trastuzumab.

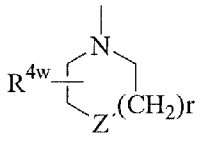
33-36. (Canceled)

37. (Previously presented) A compound of Claim 1, wherein R_2 is hydroxy-substituted phenyl.

38. (Previously presented) A compound of Claim 1, wherein R_2 is substituted or unsubstituted pyridinyl.

39. (Previously presented) A compound of Claim 1, wherein R_2 is substituted or unsubstituted pyrimidinyl.

40. (Previously presented) A compound of Claim 1, wherein W is



41. (Previously presented) A compound of Claim 40, wherein R^{4w} is H, r is 1, and Z is O.

42. (Previously presented) A compound of Claim 1, wherein Y is substituted or unsubstituted heterocyclyl.

43. (Previously presented) A compound of Claim 1, wherein X is a O and Y is substituted or unsubstituted heterocyclyl.

44. (Previously presented) A compound of Claim 1, wherein X is a direct link and Y is substituted or unsubstituted heterocyclyl.

45. (Previously presented) A compound of Claim 40, wherein R^{4w} is H, r is 1, Z is O, Y is substituted or unsubstituted heterocyclyl, R_1 is H, and R_2 is substituted or unsubstituted heteroaryl.

46. (Previously presented) A compound of Claim 40, wherein R^{4w} is H, r is 1, Z is O, X is O or a direct link, Y is substituted or unsubstituted heterocyclyl, R_1 is H, and R_2 is substituted or unsubstituted heteroaryl.

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